## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

MAR 2 6 2002

5.000 In re the application Small Miklos et al.

Serial No.: 10/019067

Filed: December 21, 2001

For: DIAGNOSIS OF GLUTEN SENSITIVE ENTEROPATHYAND OTHER

AUTOIMMUNOPATHIES

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Commissioner for Patents Washington, D.C. 2023 i

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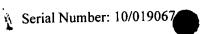
Elizabeth A. Hanley Registration No. 33,505 Attorney for Applicants

## INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their Attorney are aware of the following publications and information, listed on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration. A copy of each cited publication is enclosed.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other



relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080.

Respectfully submitted,
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Registration No. 33,505 Attorney for Applicants

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Date:\_\_

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| A1                  | $\sqcap$         | Andberg, M. et  | al. "Mutation o                            | of tyrosine 38                 | 33 in leukotriene A <sub>4</sub> h<br>ans-11,14-cis-eicosa | iydrolase i<br>atetraenoi                        | allows conve<br>c acid. Impli | cations for the   |  |  |
|                     |                  | apovide hydrol  | ase mechanist                              | n " J. <i>Biol.</i> C          | hem. 1997 Sep 12;2   | (72(37).23                                       | 007-00                        |                   |  |  |
| A2                  |                  | Barrett A.J. et   | al. Eds. "336. I                           | Introduction:                  | family M1 of membi   | ane alany  | l aminopept                   | idase," in        |  |  |
| A3                  |                  | Planeter M e  | tal "Evidence                              | for a catalyt                  | ct; pp. 994-996<br>ic role of tyrosine 38                  | 3 in the pe                                      | eptidase rea                  | ction of          |  |  |
| '``                 |                  | In ulcotriono A   | hydrolaea " <i>Eu</i>                      | r I Riocher                    | n 1995 Aug 1:231(3   | 1.020-04   |                               |                   |  |  |
| A4                  | Ţ                | Byrum, R.S. et  | al. "Determina                             | ition of the c<br>ses using 5- | ontribution of cysteir<br>lipoxygenase- and le             | eukotriene                                       | A₄ hydrolas                   | se-deficient      |  |  |
|                     |                  | mico" I Immi  | mai 1999 Dec                               | 15:163(12):                    | 6810-9   |  |                               |                   |  |  |
| A5                  | 5                | Chen, XS. et gene," Nature  | al. "Role of leu                           | ıkotrienes re                  | vealed by targeted o                                       | lisruption (                                     | or the 5-lipo                 | xygenase          |  |  |
| A6                  | 3                | Crameri A et  | al, "DNA shuffl                            | ing of a fam                   | ily of genes from div                                      | erse spec  | ies accelera                  | tes directed      |  |  |
|                     |                  | evolution," <i>Nature</i> 1998 Jan 15;391(6664):288-91  Devchand, P.R. et al. "The PPARalpha-leukotriene B₄ pathway to inflammation control," <i>Nature</i> |  |                                |  |  |                               |                   |  |  |
| A                   | 7                | 1006 Nov 7:38   | M/66041-39-43                              |                                |  |  |                               |                   |  |  |
| A                   | В                | Dittmann K H  | et al. "MK-886                             | 6. a leukotrie                 | ne biosynthesis inhi                                       | bitor, indu                                      | ces antiproli                 | iferative effects |  |  |
| -                   | +                | and apoptosis   | in HL-60 cells,                            | " Leuk. Res                    | . 1998 Jan;22(1):49-<br>with drugs modifying               | the leuk   | otriene pathy                 | way," N. Engl.    |  |  |
| A <sup>s</sup>      | "                | 4 841 4000  | Inn 24-240/21-                             | 107-206                        |  |  |                               |                   |  |  |
| A                   | 10               | Evans LE "  | eukotriene A.                              | A poor subs                    | trate but a potent int<br>1985 Sep 15;260(20               | nibitor of ra<br>0)·10966-7                      | at and huma<br>'0             | in neutrophii     |  |  |
|                     | 11               | Ford Hutchins   | on AW et al                                | "Leukotrien                    | e B. a potent chemo:                                       | kinetic and                                      | aggregaun                     | g substance       |  |  |
| ^                   |                  | released from   | polymorphopu                               | iclear leukoo                  | vtes." Nature 1980 J                                       | July 17;20                                       | 0,204-00                      |                   |  |  |
| Α                   | 12               | Not Acad Sc   | si 1194 1987 O                             | nct:84(19):66                  | amino acid sequenc   |  |                               |                   |  |  |
|                     | 13               | Griffiths R.J   | et al. "Leukotri                           | ene B <sub>4</sub> plays       | a critical role in the                                     | progression                                      | on of collage                 | en-induced        |  |  |
|                     |                  | arthritic " Proc  | · Nati Acad S                              | ci IISA 199                    | 5 Jan 17;92(2):517-2<br>thritis is reduced in 5            | ۷۱   |                               |                   |  |  |
| \ \ \ <sup>A</sup>  | 14               | Griffiths, R.J.   | et al. "Collager<br>." <i>J. Exp. Med.</i> | n-inquced ar<br>. 1997 Mar 1   | 7;185(6):1123-9  | -iiboxydei                                       | idoc dolivat                  |                   |  |  |
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| B2<br>B3<br>B4<br>B5 | Hogg, J.H. et al. "P synthetic inhibitors, Kuchner, O. et al. "Dec;15(12):523-30  Labaudinière, R. et inhibitors to LTB <sub>4</sub> relation to patt | " Chem. Eur. J. 1996 Directed evolution of t al. "ω -[(ω-Arylalkyleceptor antagonists, Leukotrienes and othershology in human of | and mechanisms of log;4(9):1698-1713  f enzyme catalysts,"  Othienyl]alkanoic acid  of J. Med. Chem. 1992  fier products of the 5-  liseases." N. Engl. J. | Trends Bio<br>ls: from spe<br>2 Aug 21;3<br>lipoxygena<br>Med. 1990 | technol. 199<br>ecific LTA <sub>4</sub> h;<br>5(17):3170-9<br>se pathway.<br>) Sep 6;323( | ydrolase<br>Biocher<br>10):645- | mis<br>-55 |
| B6                   | Lorsch, J.R. et al. "   | 'In vitro evolution of I   | new ribozymes with p   | oolynucleot   | ide kinase ad   | ctivity," <i>I</i>              | vai        |
| В7                   | site-directed mutag   | genesis and zinc ana   | olase: determination<br>lysis," <i>Proc. Natl. Ac</i>  | ad. Sci. US   | .д 1991 бер   |                                 | S D        |
| B8                   | leukotriene A₄ hydi<br>2):687-91  | rolase and metallope   | of Bacillus anthracis<br>ptidase inhibitors," <i>B</i>   | iochem. J.  | 1996 Dec 1;   | 320 ( PI                        | :          |
| В9                   | Mueller, M.J. et al.  | inactivation." Proc  | rolase: mapping of a<br>Natl. Acad. Sci. USA   | 1995 Aug :  | 29;92(18):83  | 83-1                            |            |
| B10                  | Mueller, M.J. et al.  | "Leukotriene A₄ hyd<br>e-378 " <i>Proc. Natl. A</i>  | rolase: protection fro<br><i>cad. Sci. USA</i> 1996  | m mechan<br>Jun 11;93(  | ism-based in<br>12):5931- <u>5</u>  | activatio                       |            |
| B11                  | Mueller M.I. et al.   | "Leukotriene A <sub>4</sub> hyd<br>an isomer of leukotr  | rolase, mutation of ty   | rosine 378  | allows conv   | ersion o<br>24345-8             | at<br>3    |

Examiner Date Considered

Chem. 1991 Sep 5;266(25):16507-11

receptor domain," Nat. Biotechnol. 1997 Aug;15(8):772-7

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Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Nord, K. et al. "Binding proteins selected from combinatorial libraries of an alpha-helical bacterial

aminopeptidase of high efficiency and specificity," J. Biol. Chem. 1994 Apr 15;269(15):11269-73

Orning, L. et al. "Inhibition of leukotriene A<sub>4</sub> hydrolase/aminopeptidase by captopril," J. Biol.

Orning, L. et al. "The bifunctional enzyme leukotriene- A4 hydrolase is an arginine

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| OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)  OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)  Others, C. et al. "The leukotriene B <sub>4</sub> receptor functions as a novel type of coreceptor mediating entry of primary HIV-1 isolates into CD4-positive cells." PNAS. USA 1998 Aug 4:95(16):9530-4  Rola-Pleszczynski, M. et al. "Leukotrienes augment interleukin 1 production by human monocytes," J. Immunol. 1985 Dec;135(6):3958-61  Samuelsson, B. *Leukotrienes: mediators of immediate hypersensitivity reactions and inflammation." Science 1983 May 6;220(4597):568-75  C4 Samuelsson, B. et al. "Leukotrienes and lipoxins: structures, biosynthesis, and biological effect Science 1987 Sep 4;237(4819):1171-6  C5 Serhan, C.H. et al. "Lipid mediator networks in cell signaling: update and impact of cytokines," FASEB J. 1996 Aug;10:1-12  C6 Tsuge, H. et al. "Crystallization and preliminary X-ray crystallographic studies of recombinant human leukotriene A <sub>4</sub> hydrolase complexed with bestatin," J. Mol. Biol. 1994 May 20;238(5):85  C7 Vallee, B.L. et al. "Active-site zinc ligands and activated H <sub>2</sub> O of zinc enzymes," Proc. Natl. Aca Sci. USA 1990 Jan;87(1):220-4  Wetterholm, A. et al. "Recombinant mouse leukotriene A <sub>4</sub> hydrolase: a zinc metalloenzyme with dual enzymatic activities," Biochim. Biophys. Acta 1991 Oct 25;1080(2):96-102  C9 Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A <sub>5</sub> hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," J. Pharmacol. Exp. Ther. 1995  C10 Vetterholm, A. et al. "Potent and selective inhibitors of leukotriene A <sub>5</sub> hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," J. Pharmacol. Exp. Ther. 1995  C11 Yamaoka, K.A. et al. "A G-protein-coupled receptor for leukotriene A <sub>5</sub> that mediates chemotaxis, Nature 1997 Jun 5;387(6633):620-4  C14 Yokomizo, T. et al. "A G-protein-coupled receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," J. Exp. Med. 2000 Aug 7;192(3):421-32  C14   |                     |   |  |  |  |                              | <u> </u>  |                                       |  |
| OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)  Owman, C. et al. "The leukotriene B <sub>4</sub> receptor functions as a novel type of coreceptor mediating entry of primary HIV-1 isolates into CD4-positive cells," PNAS. USA 1998 Aug 4;95(16):9530-4  C2 Rola-Pleszczynski, M. et al. "Leukotrienes augment interleukin 1 production by human monocytes," J. Immunol. 1985 Dec;135(6):3958-61  C3 Samuelsson, B. "Leukotrienes: mediators of immediate hypersensitivity reactions and inflammation," Science 1983 May 6;220(4597):568-75  C4 Samuelsson, B. et al. "Leukotrienes and lipoxins: structures, biosynthesis, and biological effect Science 1987 Sep 4;237(4819):1171-6  C5 Serhan, C.H. et al. "Lipid mediator networks in cell signaling: update and impact of cytokines," FASEB J. 1996 Aug;10:1-12  C6 Tsuge, H. et al. "Crystallization and preliminary X-ray crystallographic studies of recombinant human leukotriene A <sub>1</sub> hydrolase complexed with bestatin," J. Mol. Biol. 1994 May 20;238(5):85  C7 Vallee, B.L. et al. "Active-site zinc ligands and activated H <sub>2</sub> O of zinc enzymes," Proc. Natl. Aca Sci. USA 1990 Jan;87(1):220-4  C8 Wetterholm, A. et al. "Recombinant mouse leukotriene A <sub>4</sub> hydrolase: a zinc metalloenzyme with dual enzymatic activities," Biochim. Biophys. Acta 1991 Oct 25;1080(2):96-102  Wetterholm, A. et al. "Leukotriene A <sub>4</sub> hydrolase: abrogation of the peptidase activity by mutation of glutamic acid-296," Proc. Natl. Acad. Sci. USA 1992 Oct 1;89(19):9141-5  C10 Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A <sub>4</sub> hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," J. Pharmacol. Exp. Ther. 1995 Oct;275(1):31-7  C11 Yamoka, K.A. et al. "A G-protein-coupled receptor for leukotriene B <sub>4</sub> that mediates chemotaxis, Nature 1997 Jun 5;387(6633):620-4  C13 Yokomizo, T. et al. "A second leukotriene B <sub>4</sub> enhances activation, proliferation, and differentiation of inflammation and immunological disorders," J. Exp. Med. 2000 Aug 7;192(3):421-32  C14 Yuan, W. et al. "Novel tight-bi  |                     |   | FOREIGN PATE                                     | NT DO  | OCUMENTS   |                              |   |                                       |  |
| OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)  Owman, C. et al. "The leukotriene B <sub>4</sub> receptor functions as a novel type of coreceptor mediating entry of primary HIV-1 isolates into CD4-positive cells," <i>PNAS. USA</i> 1998 Aug 4;95(16):9530-4.  Rola-Pleszczynski, M. et al. "Leukotrienes augment interleukin 1 production by human monocytes," <i>J. Immunol.</i> 1985 Dec;135(6):3958-61  Samuelsson, B. "Leukotrienes: mediators of immediate hypersensitivity reactions and inflammation," <i>Science</i> 1983 May 6;220(4597):568-75  Samuelsson, B. et al. "Leukotrienes and lipoxins: structures, biosynthesis, and biological effect <i>Science</i> 1987 Sep 4;237(4819):1171-6  Serhan, C.H. et al. "Lipid mediator networks in cell signaling: update and impact of cytokines," <i>FASEB J.</i> 1996 Aug;10:1-12  Tsuge, H. et al. "Crystallization and preliminary X-ray crystallographic studies of recombinant human leukotriene A <sub>4</sub> hydrolase complexed with bestatin," <i>J. Mol. Biol.</i> 1994 May 20;238(5):85  C7 Vallee, B.L. et al. "Active-site zinc ligands and activated H <sub>2</sub> O of zinc enzymes," <i>Proc. Natl. Aca Sci. USA</i> 1990 Jan;87(1):220-4  Wetterholm, A. et al. "Recombinant mouse leukotriene A <sub>4</sub> hydrolase: a zinc metalloenzyme with dual enzymatic activities," <i>Biochim. Biophys. Acta</i> 1991 Oct 25;1080(2):96-102  Wetterholm, A. et al. "Leukotriene A <sub>4</sub> hydrolase: abrogation of the peptidase activity by mutation of glutamic acid-296," <i>Proc. Natl. Acad. Sci. USA</i> 1992 Oct 1;89(19):9141-5  Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A <sub>4</sub> hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," <i>J. Pharmacol. Exp. Ther.</i> 1995 Oct:275(1):31-7  C11 Yamaoka, K.A. et al. "Leukotriene B <sub>4</sub> enhances activation, proliferation, and differentiation of human B lymphocytes," <i>J. Immunol.</i> 1989 Sep 15;143(6):1996-2000  C12 Yokomizo, T. et al. "A G-protein-coupled receptor for leukotriene B <sub>4</sub> that mediates chemotaxis, <i>Nature</i> 1997 Jun 5;387(6633):620-4  Yuan, W. et al. "Novel tight-binding inhibitors of leukotr                |                     | DOCUMENT NUMBER                           | DATE   |  | COUNTRY  | CLASS                        | SUBCLASS  | TRANSLATIO                            |  |
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| monocytes," <i>J. Immunol.</i> 1985 Dec;135(6):3958-61  Samuelsson, B. "Leukotrienes: mediators of immediate hypersensitivity reactions and inflammation," <i>Science</i> 1983 May 6;220(4597):568-75  C4 Samuelsson, B. et al. "Leukotrienes and lipoxins: structures, biosynthesis, and biological effect <i>Science</i> 1987 Sep 4;237(4819):1171-6  C5 Serhan, C.H. et al. "Lipid mediator networks in cell signaling: update and impact of cytokines," <i>FASEB J.</i> 1996 Aug;10:1-12  C6 Tsuge, H. et al. "Crystallization and preliminary X-ray crystallographic studies of recombinant human leukotriene A, hydrolase complexed with bestatin," <i>J. Mol. Biol.</i> 1994 May 20;238(5):85  C7 Vallee, B.L. et al. "Active-site zinc ligands and activated H <sub>2</sub> O of zinc enzymes," <i>Proc. Natl. Aca Sci. USA</i> 1990 Jan;87(1):220-4  Wetterholm, A. et al. "Recombinant mouse leukotriene A, hydrolase: a zinc metalloenzyme wit dual enzymatic activities," <i>Biochim. Biophys. Acta</i> 1991 Oct 25;1080(2):96-102  C9 Wetterholm, A. et al. "Leukotriene A, hydrolase: abrogation of the peptidase activity by mutatio of glutamic acid-296," <i>Proc. Natl. Acad. Sci. USA</i> 1992 Oct 1;89(19):9141-5  C10 Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A, hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," <i>J. Pharmacol. Exp. Ther.</i> 1995 Oct;275(1):31-7  C11 Yamaoka, K.A. et al. "Leukotriene B <sub>4</sub> enhances activation, proliferation, and differentiation of human B lymphocytes," <i>J. Immunol.</i> 1989 Sep 15;143(6):1996-2000  C12 Yokomizo, T. et al. "A Second leukotriene B <sub>4</sub> receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," <i>J. Exp. Med.</i> 2000 Aug 7;192(3):421-32  C14 Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A <sub>4</sub> hydrolase," <i>J. Am. Chem. Soc.</i> 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human   |                     | entry of primary H                        | V-1 isolates into                                | CD4-p  | ositive cells," PIVAS.   | . <i>USA</i> 199             | tion by hum                                       | (16).9530 <u>-4</u><br>lan            |  |
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| Serhan, C.H. et al. "Lipid mediator networks in cell signaling: update and impact of cytokines," FASEB J. 1996 Aug;10:1-12  C6 Tsuge, H. et al. "Crystallization and preliminary X-ray crystallographic studies of recombinant human leukotriene A₄ hydrolase complexed with bestatin," J. Mol. Biol. 1994 May 20;238(5):85  C7 Vallee, B.L. et al. "Active-site zinc ligands and activated H₂O of zinc enzymes," Proc. Natl. Aca Sci. USA 1990 Jan;87(1):220-4  C8 Wetterholm, A. et al. "Recombinant mouse leukotriene A₄ hydrolase: a zinc metalloenzyme with dual enzymatic activities," Biochim. Biophys. Acta 1991 Oct 25;1080(2):96-102  C9 Wetterholm, A. et al. "Leukotriene A₄ hydrolase: abrogation of the peptidase activity by mutation of glutamic acid-296," Proc. Natl. Acad. Sci. USA 1992 Oct 1;89(19):9141-5  C10 Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A₄ hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," J. Pharmacol. Exp. Ther. 1995 Oct;275(1):31-7  C11 Yamaoka, K.A. et al. "Leukotriene B₄ enhances activation, proliferation, and differentiation of human B lymphocytes," J. Immunol. 1989 Sep 15;143(6):1996-2000  C12 Yokomizo, T. et al. "A G-protein-coupled receptor for leukotriene B₄ that mediates chemotaxis, Nature 1997 Jun 5;387(6633):620-4  C13 Yokomizo, T. et al. "A second leukotriene B₄ receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," J. Exp. Med. 2000 Aug 7;192(3):421-32  C14 Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A₄ hydrolase," J. Am. Chem. Soc. 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human   | "                   | Science 1987 Sep                          | 4;237(4819):117                                  | 37(4819):1171-6  |  |                              |   |                                       |  |
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| dual enzymatic activities," <i>Biochim. Biophys. Acta</i> 1991 Oct 25;1080(2):96-102  Wetterholm, A. et al. "Leukotriene A <sub>4</sub> hydrolase: abrogation of the peptidase activity by mutatio of glutamic acid-296," <i>Proc. Natl. Acad. Sci. USA</i> 1992 Oct 1;89(19):9141-5  C10 Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A <sub>4</sub> hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," <i>J. Pharmacol. Exp. Ther.</i> 1995 Oct;275(1):31-7  Yamaoka, K.A. et al. "Leukotriene B <sub>4</sub> enhances activation, proliferation, and differentiation of human B lymphocytes," <i>J. Immunol.</i> 1989 Sep 15;143(6):1996-2000  C12 Yokomizo, T. et al. "A G-protein-coupled receptor for leukotriene B <sub>4</sub> that mediates chemotaxis, <i>Nature</i> 1997 Jun 5;387(6633):620-4  C13 Yokomizo, T. et al. "A second leukotriene B <sub>4</sub> receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," <i>J. Exp. Med.</i> 2000 Aug 7;192(3):421-32  C14 Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A <sub>4</sub> hydrolase," <i>J. Am. Chem. Soc.</i> 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human  Examiner  Date Considered  | '                   | Sci. USA 1990 Jai                         | n;87(1):220-4                                    |  |  |                              | _   |                                       |  |
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| C10 Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A4 hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," <i>J. Pharmacol. Exp. Ther.</i> 1995 Oct;275(1):31-7  C11 Yamaoka, K.A. et al. "Leukotriene B4 enhances activation, proliferation, and differentiation of human B lymphocytes," <i>J. Immunol.</i> 1989 Sep 15;143(6):1996-2000  C12 Yokomizo, T. et al. "A G-protein-coupled receptor for leukotriene B4 that mediates chemotaxis, <i>Nature</i> 1997 Jun 5;387(6633):620-4  C13 Yokomizo, T. et al. "A second leukotriene B4 receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," <i>J. Exp. Med.</i> 2000 Aug 7;192(3):421-32  C14 Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A4 hydrolase," <i>J. Am. Chem. Soc.</i> 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human  Examiner  Date Considered  | "                   | of glutamic acid-2                        | 96," Proc. Natl. Ad                              | cad. S   | ci. USA 1992 Oct 1;  | 89(19): <u>91</u>            | 41-5  |                                       |  |
| Oct;275(1):31-7  C11 Yamaoka, K.A. et al. "Leukotriene B <sub>4</sub> enhances activation, proliferation, and differentiation of human B lymphocytes," <i>J. Immunol.</i> 1989 Sep 15;143(6):1996-2000  C12 Yokomizo, T. et al. "A G-protein-coupled receptor for leukotriene B <sub>4</sub> that mediates chemotaxis, <i>Nature</i> 1997 Jun 5;387(6633):620-4  C13 Yokomizo, T. et al. "A second leukotriene B <sub>4</sub> receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," <i>J. Exp. Med.</i> 2000 Aug 7;192(3):421-32  C14 Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A <sub>4</sub> hydrolase," <i>J. Am. Chem. Soc.</i> 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human  Date Considered   | C10                 | Wetterholm A et                           | al. "Potent and se                               | elective   | e inhibitors of leukoti  | riene A₄ h                   | ydrolase: efl                                     | tects on<br>ner. 1995                 |  |
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| Nature 1997 Jun 5;387(6633):620-4  Yokomizo, T. et al. "A second leukotriene B₄ receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," <i>J. Exp. Med.</i> 2000 Aug 7;192(3):421-32  Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A₄ hydrolase," <i>J. Am. Chem. Soc.</i> 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human  Examiner  Date Considered   | 042                 | human B lymphod                           | ytes," J. Immunol                                | i. 1989  | Sep 15;143(6):1996   | o-2000<br>ne.B. tha          | t mediates o                                      | hemotaxis                             |  |
| Yokomizo, T. et al. "A second leukotriene B <sub>4</sub> receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," <i>J. Exp. Med.</i> 2000 Aug 7;192(3):421-32  Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A <sub>4</sub> hydrolase," <i>J. Am. Chem. Soc.</i> 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human  Examiner  Date Considered  | C12                 | Nature 1997 Jun S                         | 5:387(6633):620-4                                | 4  |  |                              |   |                                       |  |
| inflammation and immunological disorders," <i>J. Exp. Med.</i> 2000 Aug 7;192(3):421-32  Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A₄ hydrolase," <i>J. Am. Chem. Soc.</i> 1992 April;114:6552-53  C15 GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human  Examiner  Date Considered  *EXAMPLED: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through   | C13                 | Yokomizo, T. et a                         | . "A second leuko                                | otriene  | B <sub>4</sub> receptor, BLT2.                                       | A new the                    | rapeutic tare                                     | get in                                |  |
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| *EXAMPLE D. Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through  | C15                 | GenPept Acc. No                           | S65947; leukotri                                 | iene-A   | 4 hydrolase (EC 3.3  | .2.6) long                   | isoform - hu                                      | ıman                                  |  |
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